UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,165	09/07/2004	Sudhirdas K. Prayaga	Cura 85 CON	6533

37887 7590 10/31/2006

CURAGEN CORPORATION
322 EAST MAIN STREET
BRANFORD, CT 06405

EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,165	PRAYAGA ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,8,9,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 8-9, 12-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 8/3/06 have been entered. Claims 2-4, 6-7, 10-11 and 14 are canceled. Claims 1, 5, 8-9, and 12-13 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Newly amended claim 1, and claims 8-9 and 12-13 which depend on claim1, are directed in part to an invention that is independent or distinct from the invention originally claimed for the following reasons. Claim 1 was originally drawn to an isolated nucleic acid molecule encoding a polypeptide. Newly amended claim 1 now recites an isolated nucleic acid molecule encoding a polypeptide **or** a nucleic acid molecule comprising the complement of the nucleic acid molecule encoding the polypeptide. A nucleic acid molecule which encodes a polypeptide and a complement of that sequence, while being related products, are patentably distinct in that each molecule has different chemical, structural, and functional properties, and is used for substantially different purposes. In particular, it is noted that a vector comprising a nucleic acid encoding a polypeptide can be used to produce the polypeptide in cells in vitro or in vivo. A vector comprising a complement is incapable of producing the polypeptide and if, as suggested in the specification, it is an antisense nucleic acid, it would potentially prevent or reduce the production of any endogenous polypeptide from being produced. As such, the properties of the

two molecules are not related and thus the search and examination of nucleic acid encoding a polypeptide and vectors and pharmaceutical compositions comprising a nucleic acid molecule encoding a polypeptide is not coextensive with that for nucleic acid comprising a complement or "antisense" nucleic acid sequence. Thus, the search and examination of both inventions would place an undue burden on the examiner.

Since applicant has received an action on the merits for the originally presented invention of a nucleic acid molecule encoding a polypeptide, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1, 8-9, and 12-13 are withdrawn in part from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

It is acknowledged that the applicant has amended the first paragraph of the specification to update the status of parent application 09/689,486.

Claim Rejections - 35 USC § 112

The rejection of previously pending claims 1-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in view of the cancellation of claims 2-4, 6-7, 10-11, and 14, and further in view of the amendments to the remaining claims.

The rejection of previously pending claims 1-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn over canceled claims 2-4, 6-7, 10-11 and 14, withdrawn over claims 1, 5, and 8-9 in view of the amendments to these claims, and maintained over claims 12-13. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the claims as amended are no longer directed variants or fragments of the amino acid sequence of SEQ ID NO:5, or to methods of treating or preventing NOV-associated disorders, and that the specification provides enablement for making and using the nucleic acids as claimed without undue experimentation. In response, claims 1, 5, and 8-9 have been withdrawn from this rejection. However, claims 12-13 continue to recite a pharmaceutical composition and a kit comprising said pharmaceutical composition. As discussed in detail in the previous office action, the specification does not provide any pharmaceutical use for the claimed compositions or kits aside from the treatment of NOV-associated disorders, and the specification as filed does not provide an enabling disorder for the use of the claimed nucleic acids *in vivo* to treat or prevent any disease or condition, including a "NOV-associated disorder". The applicant has not addressed any of the specific reasoning and evidence set forth in the previous office action and reiterated below. Thus, the rejection of record over claims 12-13 is maintained.

The previous office action stated that while the specification provides a working example which describes the detection of mRNA derived from the sequence of SEQ ID NO:4 in various

normal and malignant tissues, particularly prostate cancer cell lines, the specification fails to demonstrate actual protein expression of NOV2 (EphA8) in normal or malignant cells or correlate NOV2 (EphA8) expression with any effect on cell growth or tumorigenesis either *in vitro* or *in vivo*. In addition, the specification fails to provide any guidance as to "NOV-associated" disorders. Based on the known activities of ephrin receptors in development, the specification hypothesizes that NOV2 would be useful for treating neurological, cardiac and vascular pathologies. However, it is noted that neither the prior art nor the specification actually identifies any pathology or disease which is directly affected by the expression or lack or expression of any ephrin receptor. Further, while the specification does observe increased levels of NOV2 mRNA is certain cancer cell lines, the specification fails to correlate the overexpression of NOV2 with the process of tumorigenesis. The specification also fails to provide any guidance for treating cancer using a NOV2 polypeptide or nucleic acid encoding a NOV2 polypeptide. The specification does not provide any guidance as to the properties or activities of the NOV2 polypeptide that would suggest that the addition of NOV2 polypeptide to cancer cells which already overexpress NOV2 mRNA would result in any effect on cancer growth or metastasis. The applicant is reminded that "case law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves." *In re Gardner* 166 USPQ 138 (CCPA) . In the absence of specific information as to the actual biological properties of NOV2 and the identity of diseases or conditions which are directly attributable to NOV2 expression or lack of expression, it would have required undue experimentation for the skilled artisan to identify NOV2 associated diseases.

Furthermore, in regards to the administration of nucleic acids *in vivo*, at the time of filing *in vivo* gene therapy utilizing the direct administration of recombinant nucleic acids was considered to be highly unpredictable. Verma et al. states that, "[t]he Achilles heel of gene therapy is gene delivery..", and that, "most of the approaches suffer from poor efficiency of delivery and transient expression of the gene" (Verma et al. (1997) Science, Vol. 389, page 239, column 3, paragraph 2- see IDS). Marshall concurs, stating that, " difficulties in getting genes transferred efficiently to target cells- and getting them expressed- remain a nagging problem for the entire field", and that, "many problems must be solved before gene therapy will be useful for more than the rare application" (Marshall (1995) Science, Vol. 269, page 1054, column 3, paragraph 2, and page 1055, column 1, see IDS). Orkin et al. further states in a report to the NIH that, " .. none of the available vector systems is entirely satisfactory, and many of the perceived advantages of vector systems have not been experimentally validated", and that, "[w]hile the expectations and the promise of gene therapy are great, clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol" (Orkin et al. (1995) "Report and recommendations of the panel to assess the NIH investment in research on gene therapy", page 1, paragraph 3, and page 8, paragraph 2-see IDS BI-1). Among the many factors that the art teaches affect efficient gene delivery and sustained gene expression are anti-viral immune responses, and the identity of the promoter used to drive gene expression. Thus, the art at the time of filing clearly establishes that expectation for achieving a desired therapeutic effect *in vivo* by expressing a therapeutic gene using any of the expression constructs known in the art at the time of filing was extremely low.

Therefore, in view of the art recognized unpredictability in treating disease by administering nucleic acids at the time of filing, the absence of specific information as to the actual biological properties of NOV2, the lack of guidance concerning the identity of diseases or conditions which are directly attributable to NOV2 expression or lack of expression, the lack of working examples demonstrating any therapeutic effect on any disease or pathology following the administration of a nucleic acid encoding a NOV2 polypeptide, and the breath of the claims, it would have required undue experimentation for the skilled artisan to treat any and all pathological conditions including cancer by administering a nucleic acid encoding a NOV2 polypeptide.

The rejection of previously pending claims 1-14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of the cancellation or amendment of the claims.

Claim Rejections - 35 USC § 102

The rejection of claims 1 and 5-7 under 35 U.S.C. 102(b) as being anticipated by Chan et al. (1991) Oncogene, Vol. 6 (6), 1057-1061, is maintained over claims 1 and 5 and withdrawn over canceled claims 6-7. Applicant's arguments and amendments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons discussed in detail below.

The applicant argues that the claims have been amended such that they are now limited to a nucleic acid that encodes either a mature form of an amino acid sequence of SEQ ID NO:5, a polypeptide comprising SEQ ID NO:5, or a polypeptide consisting of SEQ ID NO:5 and that Chan does not teach such a nucleic acid. In response, the claims are still broad in their recitation that the nucleic acid sequence encodes a polypeptide "comprising an amino acid sequence", emphasis added by examiner. The use of the term "an amino acid sequence" reads on any amino acid sequence within the sequences set forth in (a), (b), and (c). As such, since Chan et al. teaches a human EEK cDNA which encodes a polypeptide with an amino acid sequence that is 100% identical to a fragment of SEQ ID NO: 5, Chan et al. anticipates the instant claims. However, this rejection can be overcome by amending claim 1 to recite "polypeptide comprising **the** amino acid sequence selected from the group consisting of..".

The rejection of claims 1 and 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Park et al. (1997) Oncogene, Vol. 14, 533-542, is maintained over claims 1, 5, and 8-9 and withdrawn over canceled claims 6-7. Applicant's arguments and amendments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons discussed in detail below.

The applicant argues that the claims have been amended such that they are now limited to a nucleic acid that encodes either a mature form of an amino acid sequence of SEQ ID NO:5, a polypeptide comprising SEQ ID NO:5, or a polypeptide consisting of SEQ ID NO:5 and that Park does not teach such a nucleic acid. In response, the claims are still broad in their recitation that the nucleic acid sequence encodes a polypeptide "comprising an amino acid sequence",

emphasis added by examiner. The use of the term "an amino acid sequence" reads on any amino acid sequence within the sequences set forth in (a), (b), and (c). As such, since Park et al. teaches a full length cDNA encoding mouse EEK and an expression vector comprising the EEK cDNA operably linked to a promoter, and short segments of the mouse sequence are identical to the human sequence, Park et al. anticipates the instant claims. However, this rejection can be overcome by amending claim 1 to recite "polypeptide comprising **the** amino acid sequence selected from the group consisting of..".

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not

available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER